PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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DIARIED
ID 184691

PCT

WRITTEN OPINION

(PCT Rule 66)

	Date of mailing *(day/month/year)* - 7 MAR 2001
Applicant's or agent's file reference fp12888	**REPLY DUE** within **TWO MONTHS** from the above date of mailing

International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU00/00641	7 June 2000	8 June 1999

International Patent Classification (IPC) or both national classification and IPC
Int. Cl. [7] C07K 7/50 7/56 7/64 A61K 38/12 38/08 38/16 A61P 25/28

Applicant

THE UNIVERSITY OF MELBOURNE et al

1. This written opinion is the **first** drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:.

I	[X]	Basis of the opinion
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VII	[ ]	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: **8 October 2001**

Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**GAVIN THOMPSON** Telephone No. (02) 6283 2240

WRITTEN [redacted]ION

[redacted]ational application No.
PCT/AU00/00641

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

- [X] the international application as originally filed.
- [ ] the description, pages , as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the claims, pages , as originally filed,
  pages , as amended under Article 19,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the drawings, pages , as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- [ ] contained in the international application in printed form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**3-23, 26-30, 35, 36, 39, 40, 44, 45, 50, 51**	**YES**
	Claims	**1, 2, 24, 25, 31-34, 37, 38, 41-43, 46-49, 52**	**NO**
Inventive step (IS)	Claims	**3-23, 26-30, 35, 36, 39, 40, 44, 45, 50, 51**	**YES**
	Claims	**1, 2, 24, 25, 31-34, 37, 38, 41-43, 46-49, 52**	**NO**
Industrial applicability (IA)	Claims	**1-52**	**YES**
	Claims		**NO**

2. Citations and explanations

NOVELTY (N) Claims 1 and 2

(D1) Journal Of Neurochemistry, Volume 70, No. 4, 1998 (Lippincott-Raven Publishers, Philadelphia), P. D. O'Leary and R. A. Hughes, "Structure-Activity Relationships of Conformationally Constrained Analogues of Loop 2 of Brain-Derived Neurotrophic Factor", pages 1712 to 1721.

(D2) WO 95/21193 A (MCGILL UNIVERSITY)

(D3) EP 0476933 A (SUMITOMO PHARMACEUTICALS CO. LTD.)

(D4) US 5438121 A (MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN e. V. and REGENERON PHARMACEUTICALS, INC.)

(D5) WO 97/45135 A (REGENERON PHARMACEUTICALS, INC.)

(D6) Patent Abstracts of Japan, JP 11056386 A (SUMITOMO PHARMACEUTICAL CO. LTD.)

D1 discloses BDNF-like analogues based on loop 2 (of 4) of BDNF (see the abstract, "Molecular modelling" on page 1715, and Table 1).

D2 discloses cyclic peptides capable of binding BDNF receptors (see page 5 lines 21 to 25, and page 6 line 31 to page 8 line 16).

D3 discloses cyclic brain derived neutrotrophic peptides of the hippocampal cholinergic neutrotrophic (HCNP) variety (page 4 lines 40,41 and page 11, examples 21 to 24).

D4 discloses BDNF which, of course, anticipates these broad claims to cyclic compounds with activity of BDNF.

D5 discloses BDNF in solution with surfactant which can be lypohilized (claim 15).

D6 discloses a reduced and consequently water soluble BDNF.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

INVENTIVE STEP (IS) Claims 1, 2

As above.

NOVELTY (N) ACKNOWLEDGED Claim 18

D1 discloses peptide analogues that model loop 2, not loop 4, of BDNF. D2 cyclic peptides are derived from Nerve Growth Factor (NGF). See page 5 line 35 to page 6 line 2. D3 discloses cyclic peptides of the HCNP variety. D4 to D6 describe whole BDNF peptides.

INVENTIVE STEP (IS) ACKNOWLEDGED Claim 18

above.

NOVELTY (N) Claim 23

D3 shows the readily contemplated interchange of dextrorotatory amino acids for general ones. See page 5 lines 10, 17, 26 and so on for D-Ala as an alternative for Ala in the HCNP peptide of formula (I).

INVENTIVE STEP (IS) Claim 23

It would be obvious to the person skilled in the art to substitute D-amino acids for any of the general ones in the cyclic peptides which anticipate the BDNF-like cyclic peptides of claim 1.

NOVELTY (N) Claims 24, 25

D1 discloses that the peptide analogues had cysteine residues incorporated in them that were not found in the native [redacted]p 2. See the footnote to Table 1 on page 1716. D2 shows that some conservative substitutions are permitted in the cyclic peptides. See page 8 lines 12 to 14. D3 shows amino acid substitutions and cyclisations via disulphide bonds or amide bonds on side chains are permitted. See page 4 lines 46 to 49. D4 allows conservative changes to amino acids in BDNF. See column 27 line 47 to column 28 line 19.

INVENTIVE STEP (IS) Claim 24,25

The disclosures as above render these claims lacking invention. But the changes envisaged even without the disclosures would be obvious to the person skilled in the art for the cyclic peptides nominated in D1 to D6 to anticipate the BDNF-like peptides of claim 1.

Continued...

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

NOVELTY (N) Claims 31 to 34, 37, 38, 41 to 43, 46, 47 to 49 and 52.

D1 discloses cyclic peptides that are competitive antogonists of BDNF receptors. See abstract. D2 discloses those that inhibit neutrotrophin receptors including BDNF receptors. See abstract. D3 discloses those that treat neurodegenerative diseases. See page 3 lines 5 to 7. D4 discloses that BDNF peptides treat Parkinson's disease and Alzheimer's disease. See the abstract. D5 discloses aqueous or a lypohilized BDNF containing pharmaceutical. See the abstract. D6 discloses the regeneration of a reduced BDNF which is biologically active.

INVENTIVE STEP (IS) Claims 31 to 34, 37, 38, 41 to 43, 46, 47 to 49 and 52.

As above.